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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,641	10/27/2003	Deanna L. Kroetz	02307O-115611US	4011

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

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02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,641	KROETZ ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *47 and 49* is/are allowed.

6)☒ Claim(s) *46, 48 and 50-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114.

2. Acknowledgment is made of applicant's filing of an amendment on 10/29/07. By the amendment, claims 46-49 have been amended and claims 50-53 have been newly added. Claims 46-53 are currently pending for prosecution on the merits of the case.

3. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claims 46 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Ichihara et al. (JP 07304755).

Ichihara teaches use of compounds (e.g., RN 174398-90-4, RN 174398-91-5, RN 174398-92-6, RN 174398-93-7, etc...) or their salt, which reads on the instantly claimed

compounds of the formula 1, for the treatment of the claimed cardiovascular disease such as hypertension by modulating rennin-angiotenisn system, wherein said compound is administered in various dosage forms including oral dosage forms (i.e., tablet, capsule), see para. [0001], [0035] and Table I). Ichihara discloses that a rennin inhibitor tends to control generation of angiotensin II which works powerfully to pressure ups, such as a vasoconstrictor action and aldosterone secretion, by checking the reaction of the rennin and rennin substrate (angiotensiongen) which are called rate-determining step of the renin-angiogensin series which is a pressure-up system in the living body, and reducing generation of angiotensin I (para. [0002]).

5. Claims 46 and 48 are rejected under 35 U.S.C. 102(e) as being anticipated by Blum et al. (US 5962455).

Blum teaches use of compounds (e.g., RN 202472-67-1, RN 202472-68-2, RN 202472-69-3, RN 202472-70-6,etc...) or their salt, which reads on the instantly claimed compounds of the formula 1, for the treatment of the claimed cardiovascular disease such as hypertension or essential hypertension as well as congestive heart failure, wherein said compound is administered in dosage amounts of from about 0.1mg to about 140mg per kilograms of body weight per day and in various dosage forms including oral dosage form (abstract; column 1, line 39; column 1, line 45 thru column 3, line 15; column 7, line 51; column 8, line 52 thru column 10, line 62).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 50-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ichihara et al. (JP 07304755) or Blum et al. (US 5962455).

The teaching of Ichihara or Blum has been discussed in above 35 USC 102 (b) or (e) rejection.

However, the prior art does not disclose the underlying pharmacological mechanism of said compounds in exhibiting the specific epoxide hydrolase enzymatic activity with "an IC50 of less than 500 μM or an IC50 of less than 17.8 μM". The fact that the applicant may have discovered a new pharmacological mechanism for same compound is not considered patentably

distinctive over the prior art which are directed to the same therapeutic application (for the treatment of hypertension).

Thus, in absence of factual evidence or test indicating the criticality of the instant enzymatic activity, generally by showing that the claimed range of sHE inhibitor activity achieves unexpected results over the prior art, the examiner maintains that either Ichihara or Blum makes obvious the instant invention.

Allowable Subject Matter

7. The following is a statement of reasons for the indication of allowable subject matter: The prior art reference(s) alone or in combination (Ichihara et al. and Blum et al.) in which the rejection of record is relied upon fail(s) to teach or suggest the use of compounds recited in Table I for the treatment of hypertension. Accordingly, claims 47 and 49 are allowed.

Response to Arguments

8. Applicant's arguments filed 10/29/07 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that neither Ichihara or Blum discloses or suggests any compound that functions to inhibit sHE at all, much less with an IC50 of less than 500 μM or an IC50 of less than 17.8 μM. Applicant alleges that Ichihara or Blum does not anticipate the present claims, either expressly or inherently since Ichihara discloses benzodiazepine compounds with a strong rennin inhibitory effect where Blum discloses benzylamine compounds that bind to neuropeptide Y.

This argument is not found persuasive. Unlike the applicant's argument, there is no indication in the instant claims 46 and 48 that compounds represented by the structure must essentially exhibit the alleged enzymatic activity with "an IC50 of less than 500 μM or an IC50 of less than 17.8 μM". As indicated in the previous Office Action mailed 05/11/07 (see pages 4-5 of O.A), the prior art compounds disclosed in either Ichihara overlap with the genus of compounds represented by the claimed structure. Furthermore, the prior art compounds are taught to be useful as same purpose as the instant invention, for the therapeutic utility in reducing blood pressure and/or treating hypertension. Thus, regardless of the alleged sHE inhibiting activity of the compounds, the claimed method is clearly taught in the prior art. The fact that the applicant may have discovered a new pharmacological mechanism (sHE inhibiting activity) for a compound represented by the claimed structure is not considered patentably distinctive over the prior art which are directed to the same ultimate purpose (for the treatment of hypertension).

Anticipation under 35 USC 102 is an essentially irrebuttable question of fact, wherein the court stated that anticipation "cannot be overcome by evidence of unexpected results or teachings away in the art". *In re Malagari, 499 F.2d 1289, 182 USPQ; In re Spada, 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990); In re Fracalossi, 681 F.2d 792, 215 USPQ 569 (CCPA 1982); In re Alternpohl, 500 F.2d 1151, 183 USPQ 38 (CCPA 1974); In re Wiggins, 488 F.2d 538, 179 USPQ 421 (CCPA 1973); In re Wilder, 429 F.2d 447, 166 USPQ 545 (CCPA 1970).* Indeed, a reference might reside in a nonanalogous art and yet constitute an anticipation of a claimed invention under 35 USC 102. *In re Self, 571 F.2d 134, 213 USPQ 1 (CCPA 1982).*

In response to the applicant's argument that in "the compounds of Blum, at least one of the R groups, R1 or R3 must be greater than C20", the examiner recognizes that there is no indication in the instant claims 46 and 48 that R1 or R3 must be essentially in C1-C20. Rather, the instant claims allow for inclusion of "cycloalkyl, aryl, acyl and heterocyclic" as R1 and/or R3 substituent. Thus, the examiner determines that Blum's compounds read on the instant compounds represented by the structure formula depicted in claims 46 and 48 (when R1 and R3 are "aryl").

In response to the alleged "an IC50 of less than 500 μM or an IC50 of less than 17.8 μM", it is noted that the Patent Office is not equipped to manufacture products and then obtain prior art products and make physical comparison therewith. Thus, in absence of factual evidence or test indicating the criticality of the instant enzymatic activity, generally by showing that the claimed range of sHE inhibitor activity achieves unexpected results over the prior art, the examiner maintains that either Ichihara or Blum makes obvious the instant invention.

Conclusion

9. Claims 47 and 49 are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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